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A Randomized Comparison of the Nephrotoxicity of Iopamidol and Diatrizoate in High Risk Patients Undergoing Cardiac Angiography

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Three hundred seven high risk patients with renal impairment (serum creatinine ≥1.5 mg/dl) were randomized in a double-blind manner to either iopamidol (a nonionic, low osmolar radiocontrast agent) or diatrizoate (a conventional radiocontrast agent) at cardiac angiography with subsequent follow-up study of renal function. Baseline clinical and angiographic variables were similar in the iopamidol (n = 155) and diatrizoate (n = 152) groups.

Change in renal function after angiography was less pronounced with iopamidol compared with diatrizoate as measured by mean (± SD) increase in 24 h serum creatinine (0.11 ± 0.2 versus 0.22 ± 0.26 mg/dl, $p < 0.001$), mean maximal increase in serum creatinine (0.2 ± 0.44 versus 0.38 ± 0.73 mg/dl, $p < 0.0001$) and percent of patients with a maximal increase in serum creatinine >0.5 mg/dl (8% versus 19%, $p < 0.01$). Such differences could not be documented in diabetic patients using insulin. There was no significant difference between agents in the number of patients developing clinically severe acute renal dysfunction.

It is concluded that iopamidol is less nephrotoxic than diatrizoate in high risk patients at cardiac angiography. However, the difference in nephrotoxicity is small, of no major clinical significance in the majority of high risk patients and could not be documented in insulin-using diabetic patients. Iopamidol may be the preferred agent in certain patients with advanced renal impairment, but further study is warranted.

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Renal dysfunction due to radiocontrast media is a major cause of hospital-acquired acute renal insufficiency (1). Standard ionic radiocontrast agents used over the last few decades are the salts of negatively charged, iodinated, organic compounds. These agents have high osmolarity (1,500 to 1,800 mOsm/liter) compared with biologic solutions. In recent years, new radiocontrast agents with significantly lower osmolarity, many without ionic charge, have been introduced and become widely utilized. Of significant interest to the cardiologist, these new agents generally cause fewer hemodynamic and electrocardiographic changes during angiography than do standard contrast media (2,3).

A major question concerning these new agents is their relative nephrotoxicity. A recent large scale study (4) of patients with predominantly normal renal function suggested no difference in nephrotoxicity between iopamidol, a new agent with low osmolarity and nonionicity, and diatrizoate, a standard contrast agent. However, clinically significant contrast nephropathy usually occurs in patients with preexisting renal impairment. The goal of this randomized double-blind investigation was to compare the relative nephrotoxicity of iopamidol and diatrizoate in high risk patients with preexisting renal insufficiency undergoing cardiac angiography.

Methods

Study patients. All patients undergoing cardiac catheterization at the Mayo Clinic from February 1987 through March 1989 were considered for entry into this study. Study candidates met the following criteria: 1) preexisting renal impairment defined as a recent (obtained in nearly all patients within 48 h of catheterization) serum creatinine >1.5 mg/dl (recruitment value) with the patient not on dialysis; 2) absence of significant heart failure or severe aortic stenosis at the time of catheterization (clinical indications to consider a radiocontrast agent with low osmolarity in our laboratory); 3) the patient was not receiving medications with significant nephrotoxicity (for example, gentamicin); and 4) the patient or family was able and willing to give signed consent to participate in study.

Study protocol. Patients were generally recruited to the study the night before coronary angiography. Patients were optimally hydrated in an individual fashion at the discretion of the attending physician and angiographer. Proper hydration was individualized but generally involved unrestricted

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oral fluid intake (if not clinically deleterious) until midnight before cardiac catheterization, a procedure that maintained good urine output. Intravenous fluids were administered starting the night before cardiac catheterization if the patient was unable to maintain oral intake or begun immediately before cardiac catheterization. The amount of intravenous fluids given in the immediate pericatheterization period was individualized on the basis of clinical status. Fluid balance was monitored and recorded by nursing staff and catheterization laboratory personnel. Left ventricular end-diastolic pressure was recorded before radiocontrast administration in those patients undergoing left ventriculography. The responsible staff angiographer was able to cancel an individual patient's participation in the study if it was believed that a particular radiocontrast agent should be utilized in the context of the patient's clinical problem.

At the beginning of the cardiac catheterization procedure and before the administration of contrast material, a blood sample for measurement of the baseline serum creatinine was obtained. Patients were randomized in a double-blind manner to undergo angiography with either iopamidol (Isovue-370) or diatrizoate (Renografin-76). Patient randomization was stratified with respect to the presence of insulin-treated diabetes or recruitment serum creatinine >3 mg/dl to ensure that similar numbers of patients with these abnormalities were included in both contrast groups.

Cardiac catheterization was performed in a standard manner by either the Sones or the Judkins technique. The exact procedures performed (that is, left ventriculography, aortography, coronary angiography, bypass graft angiography, angioplasty and so on) and amount of contrast medium administered were dependent on the clinical status of the patient and at the discretion of the responsible angiographer.

On the morning after angiography, a follow-up blood sample was obtained for determination of the serum creatinine level (defined as the 24 h sample). Depending on the exact timing of cardiac catheterization and blood collection, this sample was obtained 18 to 30 h after cardiac angiography. Additional follow-up serum creatinine determinations were obtained in all patients with clinical evidence of acute renal dysfunction and at the discretion of the primary service in other patients.

Data collection and analysis. Demographic, clinical, angiographic and nephrologic data were compiled in all study patients. Alterations in renal function after angiography were measured by the change in an individual patient's serum creatinine level compared with the baseline value obtained immediately before angiography. Specifically compared between the two contrast groups were the percent of patients with a >0.5 mg/dl increase in serum creatinine at 24 h after angiography, the percent of patients with a >0.5 and >1 mg/dl maximal postangiographic increase in serum creatinine, the mean change in serum creatinine at 24 h after angiography and the mean maximal postangiographic change in serum creatinine. The maximal change in serum creatinine was defined as the largest change in serum creatinine obtained 1 to 5 days after coronary angiography compared with the baseline level. Serum creatinine levels obtained after an additional radiocontrast procedure or major surgery (that is, coronary bypass in most cases) were not considered because of the possible effects of these procedures on renal function. For example, if a patient underwent cerebral angiography 48 h after coronary angiography, serum creatinine levels obtained after cerebral angiography were not considered in determining a patient's maximal increase in serum creatinine. Multiple clinical variables (Table 1) were statistically examined to detect any influence of these variables on the change in serum creatinine in the two contrast groups.

Statistical design. Study cohort size was estimated on the basis of data from a retrospective study (5) performed at the Mayo Clinic investigating contrast nephropathy in high risk patients with baseline serum creatinine levels >2 mg/dl at cardiac angiography with diatrizoate. In this study, 30% of patients had an increment in serum creatinine >0.5 mg/dl at 1 day after angiography and 22% of patients had a maximal increase of >1 mg/dl. Assuming similar changes in serum creatinine in patients studied with diatrizoate in the current study, sample sizes necessary to detect a 50% ($p < 0.05$) difference in the degree of nephrotoxicity between diatrizoate and iopamidol were estimated. Contrast groups comprising 105 patients were estimated to yield a 90% chance of detecting a 0.25 mg/dl difference in mean creatinine at 24 h between the groups. Contrast study groups of 120 and 160 patients were estimated to yield an 80% and 90% chance, respectively, of detecting a statistical difference in the prevalence of an increase in 24 h creatinine >0.5 mg/dl.

The two sample *t* test was used to compare mean values and the Wilcoxon rank sum test to compare median values when the distribution of variables was non-Gaussian. Analysis of variance of the rank transformation of the individual changes in serum creatinine was used to multivariately analyze the change in serum creatinine as a function of contrast type, insulin-treated diabetes and recruitment serum creatinine ≥3 mg/dl. Values are expressed as mean ± SD. A p value < 0.05 was considered significant.

This study was fully approved by the Mayo Clinic Institutional Human Research Review Committee in February 1987 before the start of the study.

Results

Characteristics of study groups (Table 1). During the period from February 1987 through March 1989, 325 patients were initially recruited to participate in this study. Ten patients were excluded from randomization at the time of cardiac angiography because the angiographer believed a specific contrast agent was indicated. Eight patient recruitments represented an individual patient being recruited multiple times to the study. Only a patient's first participation in the study was considered. Thus, 307 individual patients were recruited into the study, were randomized and underwent cardiac angiography with either iopamidol or

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Table 1. Comparison of Clinical Variables for the Two Contrast Groups

	Iopamidol Group	Diatrizoate Group
Mean age (yr)	68	69
Weight (kg)	81	80
Mean body surface area (m^2)	1.92	1.91
% Male	83	80
Clinical history (% patients)		
History of heart failure	36	36
NYHA functional class at angiography		
I, II	86	84
III, IV	14	16
Hypertension	66	66
Diabetes mellitus		
Total	24	23
Insulin-treated	13	13
Coronary artery disease	94	90
Peripheral vascular disease	26	25
Medications (% patients)		
Digoxin	26	19
Diuretic drug	50	55
Beta-adrenergic blocker	37	32
Vasodilator (heart failure)	9	7
Antihypertensive agent	16	20
Aspirin	34	24
Dipyridamole	25	18
Nonsteroidal anti-inflammatory medication	6	5
Calcium channel blocker	60	66
Mannitol	5	7
Laboratory findings		
Proteinuria (2-4+, % patients)	15	12
Mean uric acid (mg/dl)	7.7	7.7
Cardiomegaly on chest roentgenogram (% patients)	23	20
Mean serum creatinine (mg/dl)		
Recruitment	2.01	2.04
Baseline	1.83	1.85
Angiography (% patients or as noted)		
Coronary angiography	99	100
Left ventriculography	55	59
Mean LVEDP (mm Hg)	23	21
Mean LVEF (%)	57	59
Angioplasty	10	7
Mean dose of contrast medium (ml)	134	144
Surgery after angiography (% patients within 5 days)	25	28

LVEDP = left ventricular end-diastolic pressure; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association.

diatrizoate. Serum creatinine levels were obtained immediately before angiography (baseline) in 305 patients (99%), 24 h after angiography in 294 patients (96%) and after 24 h but within 1 week after angiography in 191 patients (62%). After excluding patients with additional contrast study or major surgery soon after cardiac angiography, determination of the increase in 24 h serum creatinine was possible in 283 patients (92%) and increase in maximal serum creatinine in 289 patients (94%).

The mean age of the study patients was 68 years (range 34 to 90); 81% were men. One hundred fifty-five patients were randomized to cardiac angiography with iopamidol and 152 with diatrizoate. Demographic, clinical and angiographic data in both groups are shown in Table 1. There were no significant differences in any of these variables between the groups. The mean recruitment serum creatinine in the study patients was 2.02 mg/dl (range 1.5 to 8.8).

Alterations in renal function (Table 2). Mean baseline serum creatinine (obtained immediately before angiography) decreased slightly from the recruitment value to 1.84 mg/dl. This likely reflected the vigorous hydration that is recommended in most patients with renal impairment undergoing radiologic study with contrast medium. The mean increase in serum creatinine 24 h after angiography was 0.11 ± 0.2 mg/dl in patients who received iopamidol compared with 0.22 ± 0.26 mg/dl in patients who received diatrizoate, a highly significant difference ($p < 0.001$). There was a >0.5 mg/dl increase in serum creatinine at 24 h in 5% of patients receiving iopamidol compared with 11% receiving diatrizoate ($p = 0.07$). The mean maximal rise in serum creatinine after angiography was 0.20 ± 0.44 mg/dl in the iopamidol group compared with 0.38 ± 0.73 mg/dl in the diatrizoate group, a highly statistically significant difference ($p < 0.0001$). Eight percent of patients receiving iopamidol had a maximal increase in creatinine >0.5 mg/dl compared with 19% of patients receiving diatrizoate ($p < 0.01$).

Acute renal failure, defined as a maximal increase in serum creatinine >1 mg/dl, occurred in 5 patients (3%) receiving iopamidol compared with 10 (7%) receiving diatrizoate ($p = 0.16$, [NS]) (Table 2). Dialysis was necessary in two patients receiving diatrizoate and one receiving iopamidol. Clinical data regarding the 15 patients with a maximal increase in serum creatinine >1 mg/dl are outlined in Table 2.

Clinical variables and renal function. Hydrational status was monitored, with no significant differences observed between the two groups. Mean measured fluid intake the day of angiography in the iopamidol group was 2.2 liters compared with 2.3 liters in the diatrizoate group. Mean measured urine output on the day of angiography was 2 liters in both groups. In patients undergoing ventriculography, mean left ventricular end-diastolic pressure was similar in the two contrast groups (Table 1). There was no significant difference in mean contrast dose (mean dose 144 ml diatrizoate versus 134 ml iopamidol) administered to the two groups.

There was no relation of dose of contrast medium administered or baseline serum creatinine to change in serum creatinine in both contrast groups. However, there were proportionally many fewer patients with severe baseline renal dysfunction (creatinine >3 mg/dl) and these patients did tend to receive lower doses of contrast agent (correlation coefficient $r = -0.27$, $p = 0.0001$) than patients with minimal baseline renal dysfunction.

Table 2. Clinical Profile of 15 Patients With Acute Renal Failure After Angiography

Pt No.	Class NYHA	DM	Contrast Type	Contrast Dose (ml)	Creatinine (mg/dl)		Oliguria	Dialysis
					Baseline	Maximal		
1	III		D	270	1.8	8.3	+	+
2		+	I	175	2.3	5.7	+	
3	III	+	I	155	1.5	2.6		
4	III	+	D	60	2.7	3.9		
5		+	D	315	1.6	2.6		
6		+	D	115	3.6	5.3		
7		+	I	80	3.6	4.6		
8	II		D	80	4.3	7.0		
9			D	70	2.2	3.2		
10	I	+	I	90	7.1	10.5	+	+
11			D	70	6.5	8.8		+
12	III	+	D	150	2.0	3.6		
13			D	120	5.4	9.1	+	
14	IV		I	150	1.9	2.9		
15	IV		D	250	1.4	3.6		

D = diatrizoate; DM = insulin-treated diabetes mellitus; I = iopamidol; NYHA = New York Heart Association functional class—no entry in this column denotes no prior history of heart failure; Pt = patient; + = present.

The clinical variables listed in Table 1 were analyzed to determine any possible associations with maximal increase in serum creatinine after angiography in the two contrast groups. An association with maximal increase in serum creatinine was noted only in a subgroup of patients with diabetes. Diabetic patients who used insulin had a statistically greater postangiographic maximal increase in serum creatinine compared with other study patients ($p = 0.001$). Baseline renal dysfunction was greater in this subgroup (mean baseline creatinine 2.4 versus 1.76 mg/dl in others) and likely influenced the greater degree of contrast-related renal dysfunction. The degree of baseline renal dysfunction in this diabetic subgroup was equivalent in both contrast groups. In addition, there was no difference in the degree of nephrotoxicity of iopamidol compared with diatrizoate in this diabetic subgroup. In insulin-using diabetic patients, there was a mean maximal increase in creatinine after angiography of 0.6 ± 1.02 mg/dl with iopamidol compared with 0.54 ± 0.51 mg/dl with diatrizoate ($p = 0.36$ [NS]).

In the remaining study patients, there was a mean maximal increase in creatinine of 0.13 ± 0.2 mg/dl with iopamidol compared with 0.36 ± 0.76 mg/dl with diatrizoate ($p < 0.0001$). In insulin-using diabetic patients, there was a >0.5 mg/dl maximal increase in serum creatinine in 30% of the iopamidol group compared with 40% of the diatrizoate group ($p = 0.51$ [NS]). In the remaining study patients, there was a maximal increase in creatinine >0.5 mg/dl in 5% with iopamidol and 16% with diatrizoate ($p < 0.004$).

The maximal increase in serum creatinine plotted against recruitment serum creatinine is graphically displayed for the two contrast groups (Fig. 1) with respect to the presence or absence of diabetes requiring insulin. Four quadrants are constructed in each group, with divisions at recruitment serum creatinine = 3 mg/dl and maximal increase in serum creatinine = 0.5 mg/dl. In all graphs, but especially in Figure 1A and B (patients without diabetes requiring insulin), the great majority of patients are in the lower left quadrant, denoting recruitment serum creatinine levels between 1.5 and 3 mg/dl and a maximal increase in serum creatinine <0.5 mg/dl. Figure 1B is noteworthy in that no patient in this subgroup (iopamidol, no diabetes requiring insulin) had a maximal increase in serum creatinine >1 mg/dl and no patient with a recruitment serum creatinine >3 mg/dl had a maximal increase in creatinine >0.5 mg/dl.

Multivariate analysis. Analysis of variance was utilized to multivariately analyze the effects of type of contrast agent, diabetes mellitus requiring insulin and presence of severe renal insufficiency (recruitment serum creatinine >3 mg/dl) on the maximal change in serum creatinine after angiography. A greater maximal change in serum creatinine was independently related to the use of diatrizoate ($p = 0.0001$), presence of diabetes requiring insulin ($p = 0.0006$) and presence of severe preexisting renal insufficiency ($p = 0.034$).

Discussion

Iopamidol versus diatrizoate. The major finding of this study is that in patients with preexisting renal insufficiency undergoing coronary angiography, iopamidol is less nephrotoxic than is diatrizoate. The increase in 24 h serum creatinine (0.11 ± 0.20 versus 0.22 ± 0.26 mg/dl), maximal increase in serum creatinine (0.20 ± 0.44 versus 0.38 ± 0.73 mg/dl) and percent of patients with maximal increase in serum creatinine >0.5 mg/dl (8% versus 19%) were all significantly lower in the iopamidol group than in the diatrizoate group. However, this observed difference in nephrotoxicity was small when considering the absolute difference in the changes in serum creatinine between the two contrast groups, and there was no observed difference in nephrotox-

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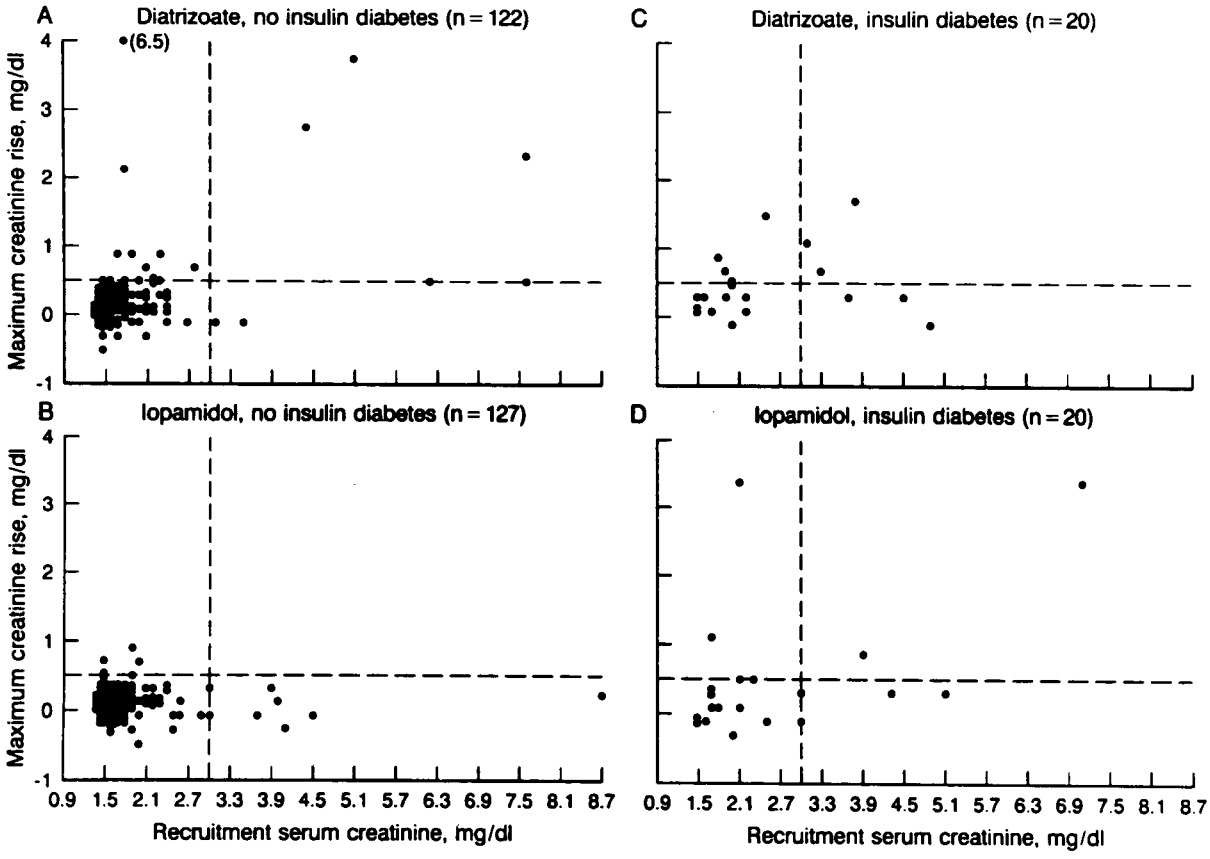

Figure 1. Maximal increase in serum creatinine plotted against recruitment serum creatinine levels for patient subgroups A (diatrizoate, no insulin-treated diabetes), B (iopamidol, no insulin-treated diabetes), C (diatrizoate, insulin-treated diabetes) and D (iopamidol, insulin-treated diabetes). **Dashed lines** are drawn at recruitment serum creatinine = 3 mg/dl (**vertical**) and maximal increase in serum creatinine = 0.5 mg/dl (**horizontal**).

icity between the contrast agents in diabetic patients using insulin. In addition, there was no statistically significant difference between the two agents in the number of patients developing pronounced renal toxicity, defined as a maximal increase in serum creatinine >1 mg/dl.

Contrast nephropathy: background. Contrast nephropathy has become an important cause of acute renal insufficiency because of the large number of radiocontrast procedures currently utilized in modern medical practice. Clinically significant contrast nephropathy is exceedingly rare in patients with normal renal function, but occurs more frequently in those with preexisting renal impairment, especially in the setting of diabetes mellitus (6–9). The exact mechanism of contrast nephropathy is uncertain and may vary in different patients. Standard iodinated contrast agents have high osmolarity and are ionic in composition. High osmolarity is postulated to be a contributing factor in contrast nephrotoxicity. Diatrizoate is the sodium and methylglucamine salt of diatrizoic acid with an osmolarity of 1,500 mOsm/liter. Several new contrast agents (including iopamidol) have significantly lower osmolarity and are without ionic charge in solution. The formulation of iopamidol (Isovue-370) utilized in this study has an osmolarity of 796 mOsm/liter.

Previous investigations. Initial laboratory and small clinical studies (<100 patients) (10–17) have reached varied conclusions in investigating the relative nephrotoxicity of the new contrast agents compared with standard agents. Recently, several large clinical studies examined the relative nephrotoxicity of ionic and nonionic contrast media in patients undergoing cardiac angiography. In patients having cardiac catheterization and angiography with iopamidol (18), 6% of patients developed a postangiographic maximal increase in creatinine >0.5 mg/dl and 1.4% a maximal increase >1 mg/dl. No patient developed oliguria or needed dialysis. Regression analysis showed that the risk of nephrotoxicity increased exponentially when the baseline serum creatinine was >1.2 mg/dl. In a second study by the same investigators (4), the degree of nephrotoxicity of iopamidol and diatrizoate was compared in a randomized trial in a general group of patients undergoing cardiac catheterization. In this study of patients with predominantly normal renal function, there was no difference in nephrotoxicity between the two agents. The investigators (4) and the authors of an accompanying editorial (19) pointed out that these findings may not apply to patients with preexisting renal insufficiency. An additional important finding in that study (4) was that heart failure and diabetes mellitus did not enhance the risk of contrast nephropathy in patients with normal renal function.

In a recent series examining the influence of diabetes and

preexisting renal influence on contrast nephropathy, the authors (20) commented that low osmolar contrast media did not appear to be less nephrotoxic compared with conventional agents. However, <30% of the patients in their study received a low osmolar contrast agent, and patients were not randomized with respect to the type of contrast agent administered. The authors (20) concluded that additional study of the nephrotoxicity of the new agents was necessary. Another recent series (21) compared low osmolar and conventional contrast media in patients with insulin-dependent diabetes mellitus undergoing high dose urography. There were no clinical differences in nephrotoxicity between the two agents in this group of patients with primarily normal renal function.

Gomes et al. (22) reported on 145 patients who underwent various angiographic procedures with the nonionic agent iohexol with follow-up study of renal function. Acute renal dysfunction (increase in serum creatinine by 50% or 1 mg/dl) occurred in 5.5% of patients. In contrast, 10% of an historical control group of 202 patients studied with a standard ionic agent developed acute renal dysfunction. The investigators (22) recommended a randomized trial to document a possible advantage of nonionic contrast media.

Present investigation. Our study was designed to examine the relative nephrotoxic effects of iopamidol and diatrizoate in a high risk group of patients studied with extreme caution in our cardiac catheterization laboratory. Our approach in such patients during the execution of this study was to implement proper hydration and to try to reduce the amount of contrast medium administered. Although the dose of contrast medium administered may not be a critical factor in patients with normal renal function (23), we (5,24) believed that large contrast doses may enhance the risk of nephrotoxicity in patients with preexisting renal insufficiency at angiography. This latter concern likely explains why the mean dose of contrast medium administered was 137 ml in our study compared with 177 and 201 ml, respectively, in the two recent studies (4,18) involving a general group of patients undergoing cardiac catheterization.

Interpretation and recommendations. Our data suggest that iopamidol is less nephrotoxic than diatrizoate in patients with preexisting renal impairment. However, this difference is small and of little clinical consequence in most patients (Fig. 1). Also, in patients with perhaps the greatest risk for contrast nephropathy, insulin-using diabetic patients with renal impairment, we were unable to determine any difference in nephrotoxicity between the two agents. This latter finding, however, should be interpreted with caution because of the overall small number of patients with insulin-treated diabetes mellitus (n = 40) included in our study. We believe that in the majority of high risk patients (serum creatinine ≥1.5 mg/dl) undergoing cardiac angiography, the risk of clinically significant renal toxicity is low when patients are properly hydrated and contrast exposure is minimized. In such patients, the type of angiographic dye administered may not be the most important factor.

Clinical considerations other than contrast nephropathy should also be weighed in the selection of contrast agent used. However, it may be prudent to consider an agent like iopamidol in patients with advanced renal impairment and very limited renal reserve in whom a relatively small detrimental effect on renal function may be of significant clinical consequence. Although there were few patients with advanced renal impairment (creatinine >3 mg/dl) in our study, this approach appears justified (Fig. 1) at least in patients without insulin-treated diabetes mellitus. Clearly, additional study of larger numbers of patients with advanced renal impairment and patients with diabetes is warranted.

The selective use of a low osmolar contrast medium is important in view of cost-containment measures in modern medical practice. Currently, the low osmolar contrast agents are approximately 7 to 15 times as expensive as standard ionic contrast media in the United States. Although the cost of contrast medium is a small fraction of the total cost of coronary angiography, we have estimated that the use of low osmolar contrast media in all patients (approximately 5,000/year) undergoing cardiac angiography at our institution would yield an additional yearly expense of approximately $900,000. The definition of subgroups in which there is a clinical advantage of low osmolar agents as well as subgroups with no clear-cut clinical advantage is important for maximization of health care resources.

Limitations. Although we studied 307 patients, this patient number was too small to completely compare the prevalence of clinically important nephrotoxicity of the two agents. The rates of clinically important nephrotoxicity were less than anticipated (see Methods), likely as a result of inclusion of patients with baseline serum creatinine levels in the 1.5 to 1.9 mg/dl range in the current study but not in the retrospective study (5) from which estimates were made. It is speculative whether greater patient numbers would have shown iopamidol to be the superior agent in this regard. Hundreds of additional patients might be required to determine such possible statistical differences; however, it is not likely that an expanded cohort of patients would dramatically alter our current conclusions.

Ideally, any study of contrast nephropathy should include baseline study of multiple variables of renal function with daily follow-up assessment of renal function in all patients for 4 to 5 days. Unfortunately, in most clinical settings, this is not practical or possible. We designed our study on the basis of data in which current clinical practice is executed. Serum creatinine was selected as the major variables of renal function because of its wide utilization and application. Additional variables of renal function were not studied because we believed that they would not yield a significant increment in clinically relevant data above that defined by serum creatinine. Patients had careful measurement of fluid balance and baseline and 24 h serum creatinine levels. Sixty-two percent of the patients had additional follow-up study of serum creatinine. Ideally, all patients should have had additional follow-up assessment of renal function. This

was not possible in many patients who had no evidence of contrast nephropathy at 24 h after angiography.

Conclusions. This investigation demonstrates that iopamidol is less nephrotoxic than diatrizoate in high risk patients undergoing cardiac angiography. However, this difference in nephrotoxicity is of little clinical consequence in the majority of high risk patients and cannot be demonstrated in insulin-using diabetic patients. Iopamidol rather than diatrizoate may be the preferred agent in patients with advanced renal impairment, although this subgroup and patients with diabetes mellitus merit further study.

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